Disorders Of The Neurohypophysis

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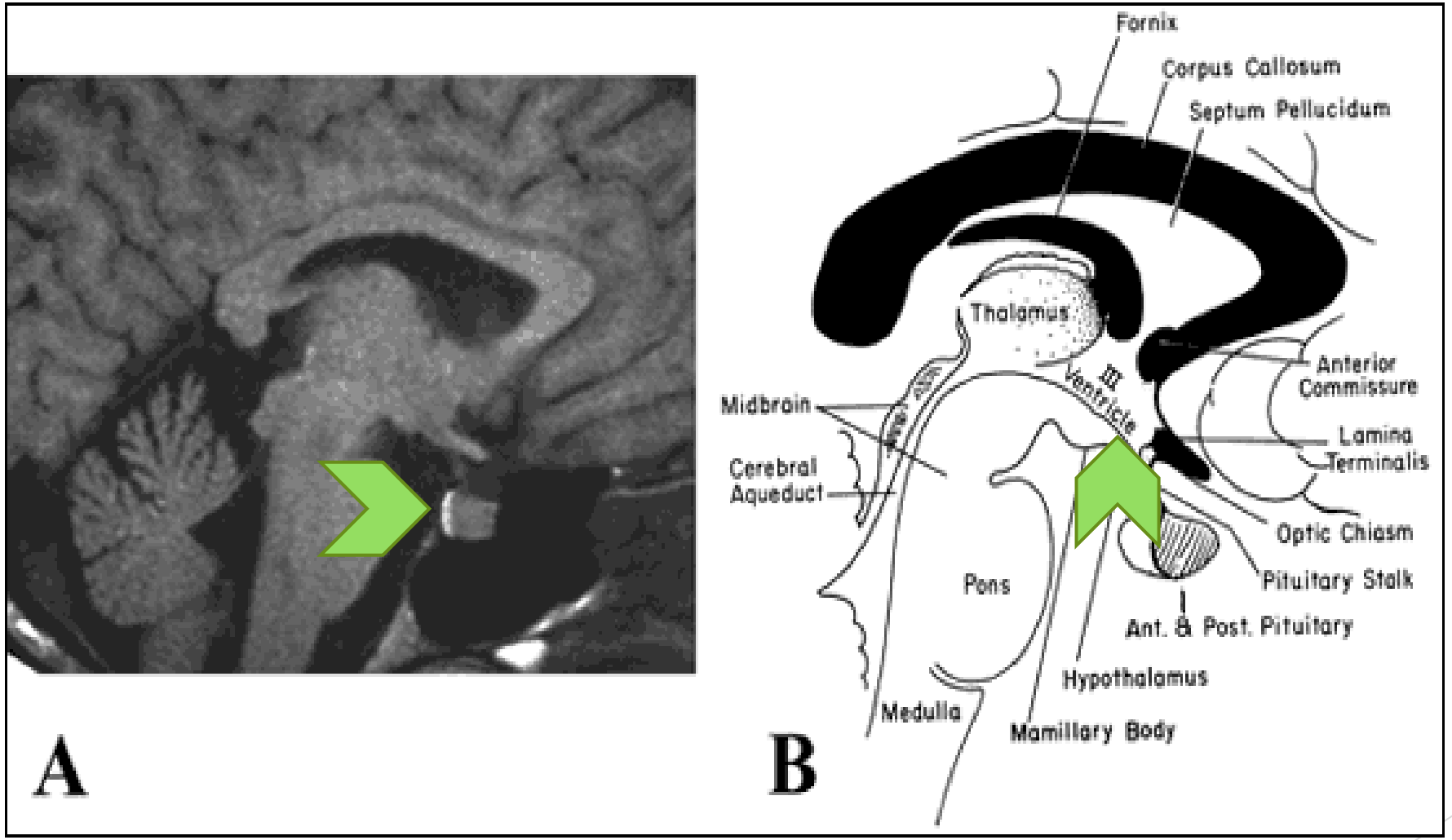
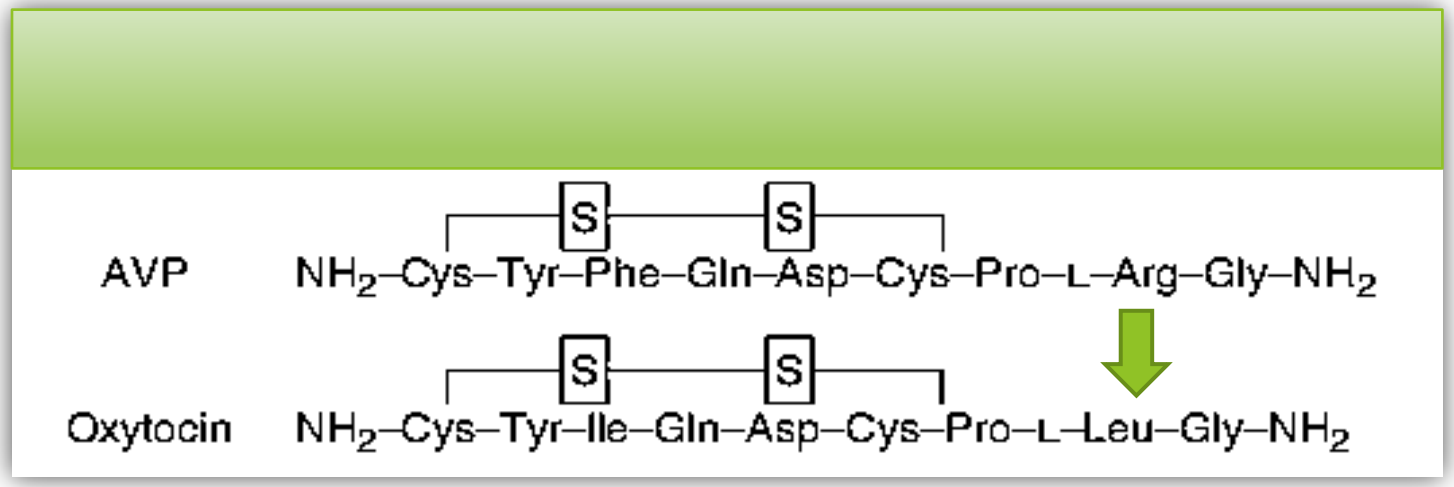
Posterior Pituitary Gland



- The posterior pituitary gland secretes :



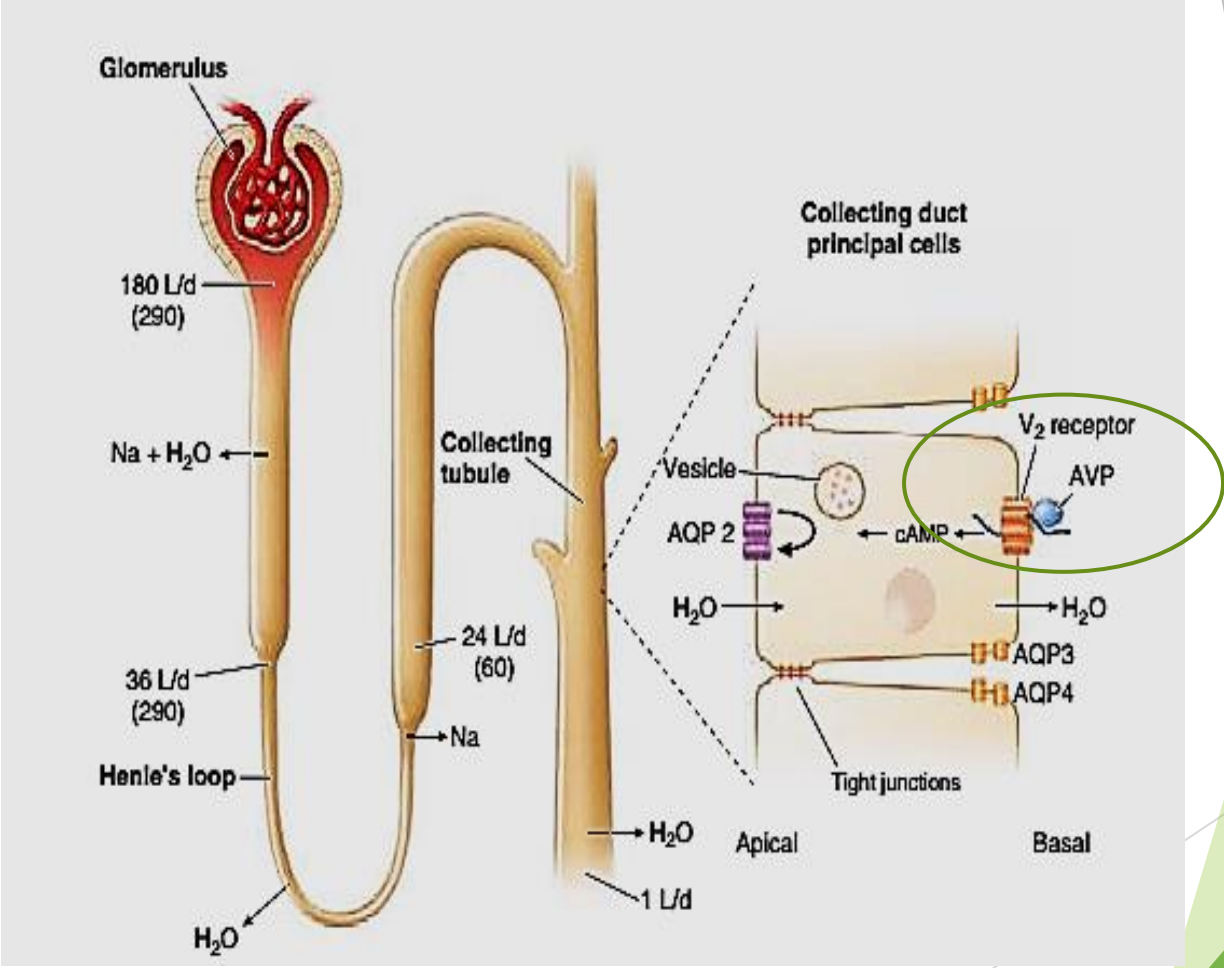
- AVP is a nonapeptide composed of a six-member disulfide ring and a tripeptide tail….

- It is synthesized via a polypeptide precursor that includes AVP, neurophysin, and co-peptin, all encoded by a single gene on chromosome 20…

- AVP secretion is regulated primarily by the “effective” osmotic pressure of body fluids…
- This control is mediated by specialized hypothalamic cells known as osmoreceptors, which are extremely sensitive to small changes in the plasma concentration of sodium and its anions but normally are insensitive to other solutes such as urea and glucose…
- It is cleared irreversibly with a half-life (t 1/2) of 10–30 min and most AVP clearance is due to degradation in the liver and kidneys…
- During pregnancy, the metabolic clearance of AVP is increased three to four fold due to placental production of an N-terminal peptidase.

- ADH binds to receptors on the renal tubule, increasing the water permeability of the luminal membrane of the collecting duct epithelium…

- This antidiuretic effect is mediated via a G protein–coupled V2 receptor that increases intracellular c-AMP, thereby inducing translocation of aquaporin 2 water channels (AQP 2) into the apical membrane …



- ADH also binds to peripheral arteriolar receptors (V1), causing vasoconstriction and resultant increase in blood pressure…

- ADH also causes bradycardia and the inhibition of sympathetic nerve activity… (a counter-effect to the hypertensive effect of ADH)

DIABETES INSIPIDUS

- Diabetes insipidus (DI) is characterized excretion of large volumes of dilute urine and caused by low secretion or action of ADH…
- DI can be:
  - Neurogenic (central)
  - Nephrogenic
  - Gestational - primary deficiency of plasma AVP can result from increased metabolism by an N-terminal amino-peptidase produced by the placenta…

Causes of Diabetes insipidus

Pituitary diabetes insipidus

- Acquired
  - Head trauma (closed and penetrating) including pituitary surgery
  - Neoplasms
    - Primary
      - Craniopharyngioma
      - Pituitary adenoma (suprasellar)
      - Dysgerminoma
      - Meningioma
    - Metastatic (lung, breast)
    - Hematologic (lymphoma, leukemia)
  - Granulomas
    - Sarcoidosis
    - Histiocytosis
    - Xanthoma disseminatum
  - Infectious
    - Chronic meningitis
    - Viral encephalitis
    - Toxoplasmosis
  - Inflammatory
    - Lymphocytic infundibuloneurohypophysitis
    - Granulomatosis with polyangiitis (Wegener's)
    - Lupus erythematosus
    - Scleroderma
  - Chemical toxins
    - Tetrodotoxin
    - Snake venom
  - Vascular
    - Sheehan's syndrome
    - Aneurysm (internal carotid)
    - Aortocoronary bypass
    - Hypoxic encephalopathy
  - Idiopathic
- Congenital malformations
  - Septo-optic dysplasia
  - Midline craniofacial defects
  - Holoprosencephaly
  - Hypogenesis, ectopia of pituitary
- Genetic

Gestational diabetes insipidus

Pregnancy (second and third trimesters)

Nephrogenic diabetes insipidus

Acquired

- Drugs
  - Lithium
  - Demeclocycline
  - Methoxyflurane
  - Amphotericin B
  - Aminoglycosides
  - Cisplatin
  - Rifampin
  - Foscarnet
- Metabolic
  - Hypercalcemia, hypercalciuria
  - Hypokalemia
- Obstruction (ureter or urethra)
- Vascular
  - Sickle cell disease and trait
  - Ischemia (acute tubular necrosis)
- Granulomas
  - Sarcoidosis
- Neoplasms
  - Sarcoma
- Infiltration
  - Amyloidosis
- Idiopathic

Genetic

- X-linked recessive *(AVP receptor-2 gene)*
- Autosomal recessive *(AQP2 gene)*
- Autosomal dominant *(AQP2 gene)*

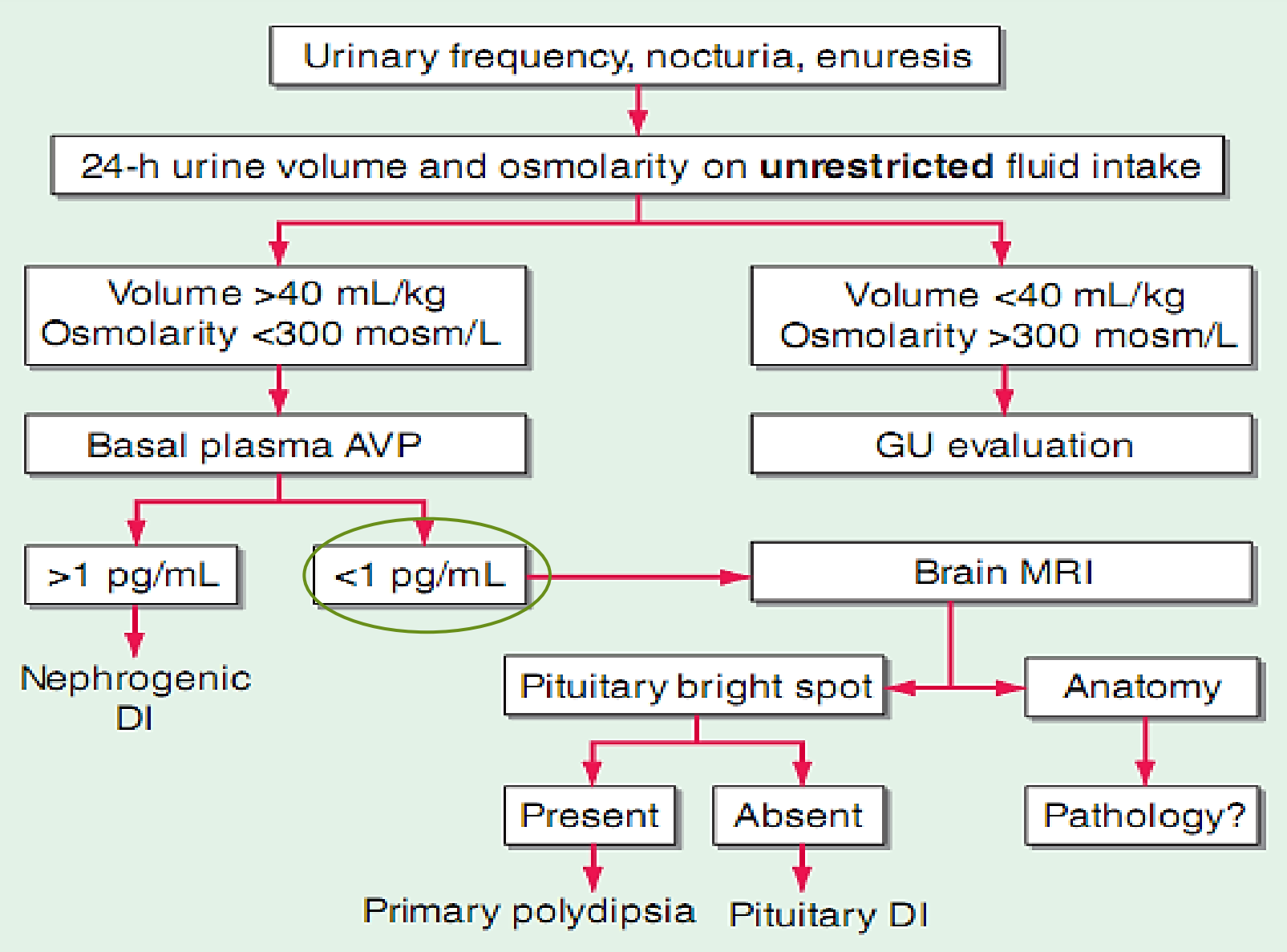
Primary polydipsia

Acquired

- Psychogenic
  - Schizophrenia
  - Obsessive compulsive disorder
- Dipsogenic (abnormal thirst)
  - Granulomas (sarcoidosis)
  - Infectious (tuberculous meningitis)
  - Head trauma (closed and penetrating)
  - Demyelination (multiple sclerosis)
  - Drugs
  - Idiopathic
  - Iatrogenic

Diagnosis…

- Regardless of the cause, patients are polyuric (50 mL/kg per day), secreting large volumes of dilute urine and this causes cellular and extracellular dehydration, stimulating thirst …
- The primary test used to differentiate the causes of polyuria is the water deprivation test.
- In diabetes insipidus (central or nephrogenic), inappropriate diuresis results in a urine osmolarity that is less than that of plasma osmolarity….
- If DI is confirmed, basal plasma arginine vasopressin (AVP) should be measured on unrestricted fluid intake…


Urinary frequency, nocturia, enuresis
24-h urine volume and osmolarity on **unrestricted** fluid intake
Volume >40 mL/kg
Osmolarity <300 mosm/L
Volume <40 mL/kg
Osmolarity >300 mosm/L
Basal plasma AVP
GU evaluation
>1 pg/mL
<1 pg/mL
Brain MRI
Nephrogenic DI
Pituitary bright spot
Anatomy
Present
Absent
Pathology?
Primary polydipsia
Pituitary DI

- If MRI and/or AVP assays with the requisite sensitivity and specificity are unavailable and a fluid deprivation test is impractical or undesirable, a third way to differentiate between pituitary DI, nephrogenic DI, and primary polydipsia is a trial of desmopressin therapy…

- Such a trial should be conducted with very close monitoring of serum sodium as well as urine output, preferably in hospital, because desmopressin will produce hyponatremia in 8–24 h if the patient has primary polydipsia…

TREATMENT…

- DDAVP acts selectively at V2 receptors to increase urine concentration and decrease urine flow …
- DDAVP can be given by IV or SC injection, nasal inhalation, or orally by means of a tablet of melt.
- Among adults, they usually range from 1–2 μg qd or bid by injection, 10–20 μg bid or tid by nasal spray, or 100–400 μg bid or tid orally…
- Primary polydipsia cannot be treated safely with DDAVP or any other antidiuretic drug because eliminating the polyuria does not eliminate the urge to drink (water intoxication…)

- Nephrogenic DI are not affected by treatment with standard doses of DDAVP, but if resistance is partial, it may be overcome by ten-fold higher doses…

- However, treatment with conventional doses of a thiazide diuretic and/ or amiloride in conjunction with a low-sodium diet and a prostaglandin synthesis inhibitor (Indomethacin) usually reduces the polyuria and polydipsia by 30–70%…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